

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant:	Ruggero FARIELLO <i>et al.</i>	Docket No:	373987-011US (102895)
Serial No.:	10/559,982	Confirmation No.:	6583
Filed:	February 2, 2006	Group Art Unit:	1627
For:	METHODS FOR TREATMENT OF PARKINSON'S DISEASE	Examiner:	Sahar JAVANMARD

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**INTERVIEW SUMMARY PURSUANT TO 37 C.F.R. § 1.137(b)**

*via EFS*

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Further to the Interview Summary Form mailed November 26, 2010, setting the latest of thirty days or one month from the interview held November 16, 2010 or the mailing date of the Interview Summary Form, or **December 26, 2010**, as the deadline for applicants to file an interview summary pursuant to 37 C.F.R. § 1.137(b), applicants provide the following remarks.

Interview Summary

A personal interview was held on November 16, 2010 attended by (i) the undersigned attorney of record, (ii) Dr. Marco Caremi, representing the assignee of the instant application, (iii) Dr. Warren Olanow, applicants' expert, and Examiners (iv) Sahar Javanmard and (v) Sreeni Padmanabhan. Two independent claim alternatives were discussed:

- A.** A method of treating idiopathic Parkinson's disease, comprising:  
orally administering safinamide, or a pharmaceutically acceptable salt thereof, on a daily dosage schedule of about 0.5 mg/kg/day to about 5 mg/kg/day to a patient with idiopathic Parkinson's disease; and  
concurrently administering levodopa, optionally with a peripheral decarboxylase inhibitor, wherein levodopa is administered in an amount that alone has therapeutic effect.
- B.** In a method of treating idiopathic Parkinson's disease in a patient receiving a stable dose of levodopa, optionally with a peripheral decarboxylase inhibitor, the improvement comprising:  
concurrently administering safinamide, or a pharmaceutically acceptable salt thereof, on an oral dosage schedule of about 0.5 mg/kg/day to about 5 mg/kg/day, without reducing the patient's dosage of concurrently administered levodopa.

Version A corresponds to pending claim 58 rewritten in independent form. Version B, presented in Jepson format, had not previously been proposed.

The patentability of each claim alternative was discussed, with the undersigned addressing the Examiner's *prima facie* case of obviousness over U.S. Pat. No. 5,017,607 (Chiesi) and U.S. Pat. No. 5,236,957 (Dostert *et al.*) and applicants' expert, Dr. Olanow, discussing new clinical trial results that evidence unexpected results. A true and complete copy of the slide presentation describing the clinical trial results is attached hereto as Exhibit A. Applicants agreed to file a Request for Continued Examination with a response to the outstanding final action and a Declaration by Dr. Warren Olanow, at which time the Examiner will reconsider the *prima facie* case and consider the unexpected results presented in the interview. No further agreement was reached.

Applicants wish to thank both Examiner Javanmard and Examiner Padmanabhan for the courtesy extended during the interview.

Respectfully submitted,

Date: December 15, 2010

/Daniel M. Becker/

Daniel M. Becker

Reg. No. 38,376

**DECHERT LLP**

**Customer No. 37509**

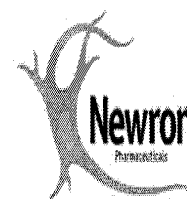
Tel: 650.813.4800

Fax: 650.813.4848

Exhibit A: Newron Pharmaceuticals SpA, "Safinamide: Study 018 Top-Line Results,"  
Investor and Analyst Call Presentation, November 4, 2010

## **Exhibit A**

**Newron Pharmaceuticals SpA, "Safinamide: Study 018 Top-Line Results,"  
Investor and Analyst Call Presentation, November 4, 2010**



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# **Newron Pharmaceuticals S.p.A.**

Investor and analyst call

**Safinamide**

**Study 018 Top-Line Results**

November 4, 2010

03.00 p.m. CET

Moderators:

Luca Benatti, CEO

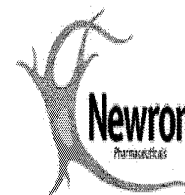
Ravi Anand, CMO

European dial-in: +39 02 805 8811

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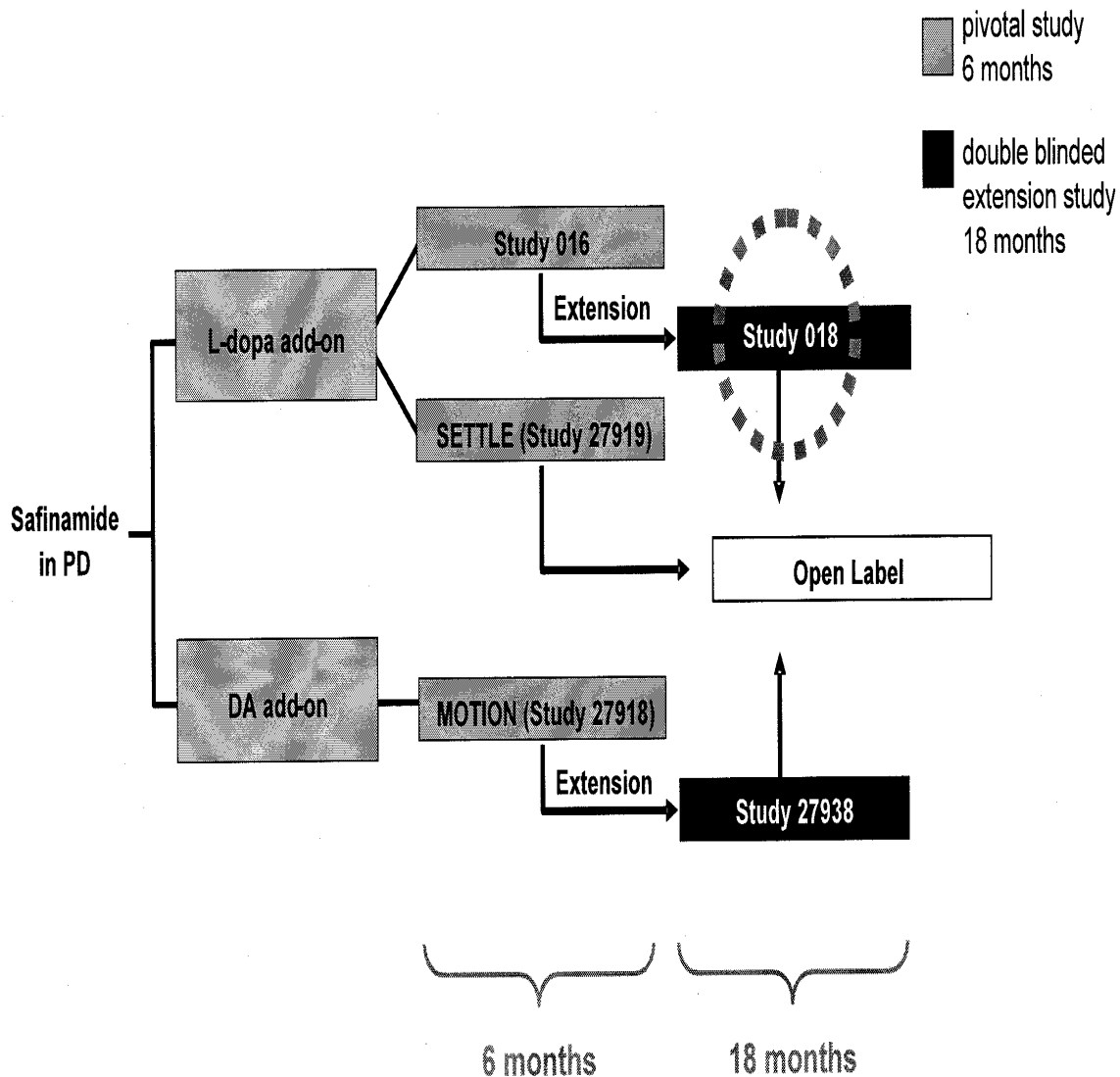
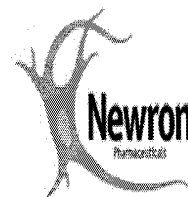
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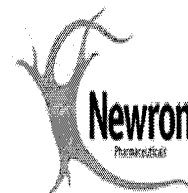
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# Safinamide Parkinson's disease - add-on program ongoing



# Study 016 - Key inclusion criteria

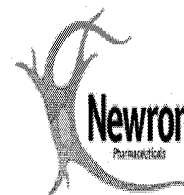
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- Male or female, aged 30-80 years
- Diagnosis of idiopathic Parkinson's Disease of > 3 yrs
- Levodopa responsive and receiving a stable dose of levodopa at screening
  - 4-10 doses per day
  - Any levodopa preparation (plus benserazide/carbidopa)
  - COMT inhibitors permitted (including Stalevo®)
- Patients may be receiving concomitant treatment with stable doses of a dopamine agonist and/or an anticholinergic
- Motor fluctuations with >1.5 hours OFF time during day
- Ability to maintain diary (18 hours) with help of caregiver
- Complete ophthalmologic screening

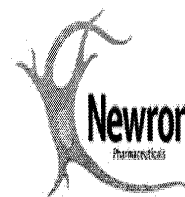


# Study 016 - Baseline subject demographics and disease characteristics



	Placebo (n=222)	Safinamide 50 mg/day (n=223)	Safinamide 100 mg/day (n=224)
Mean age (years) (SD)	59.4 (9.41)	60.1 (9.67)	60.1 (9.19)
Gender Male (%)	72.1%	70.4%	72.8%
Race			
Asian	180 (81.1%)	180 (80.7%)	179 (79.9%)
White	42 (18.9%)	43 (19.3%)	45 (20.1%)
At least one concomitant medical condition/illness	165 (74.3%)	178 (79.8%)	175 (78.1%)

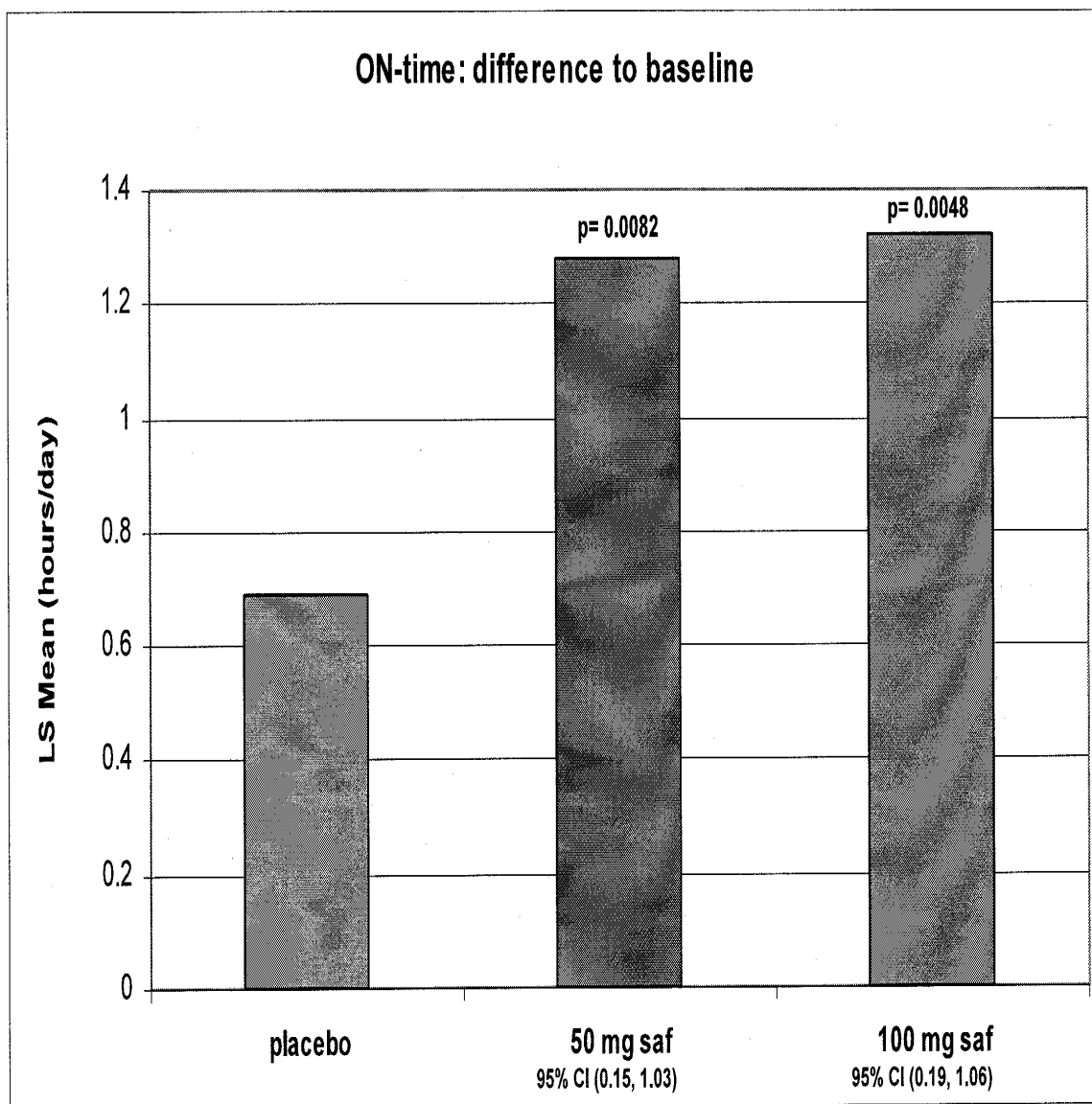
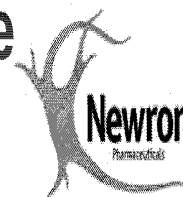
# Study 016 – Parkinson's disease baseline characteristics



	Placebo (n=222)	Safinamide 50 mg/day (n=223)	Safinamide 100 mg/day (n=224)
Baseline OFF time (hours) (SD)	5.3 (2.06)	5.2 (2.08)	5.2 (2.16)
Baseline ON time (hours) (SD)	9.30 (2.155)	9.37 (2.259)	9.52 (2.426)
Baseline UPDRS Part III ON (SD)	28.7 (12.03)	27.3 (12.67)	28.3 (13.30)
% of patients with Troublesome Dyskinesia ( $\geq 30$ mins)	32.8 %	32.3 %	29.5 %
PD Treatment			
Levodopa	222 (100.0%)	223 (100.0%)	224 (100.0%)
Dopamine Agonist	136 (61.3%)	142 (63.7%)	128 (57.1%)
Anticholinergic	86 (38.7%)	73 (32.7%)	85 (37.9%)
Entacapone	56 (25.2%)	52 (23.3%)	55 (24.65)
Stalevo	33 (14.9%)	30 (13.5%)	36 (16.1%)
Amantadine	32 (14.4%)	29 (13.0%)	30 (13.4%)

# Study 016 primary endpoint met : ON Time

*Study qualified pivotal study*

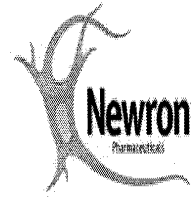


p-values were calculated using a mixed linear model based on the change from baseline with baseline as covariate

## **Study 018 objective:**

*Long-term safety and efficacy for mid-to-late stage  
Parkinson's disease*

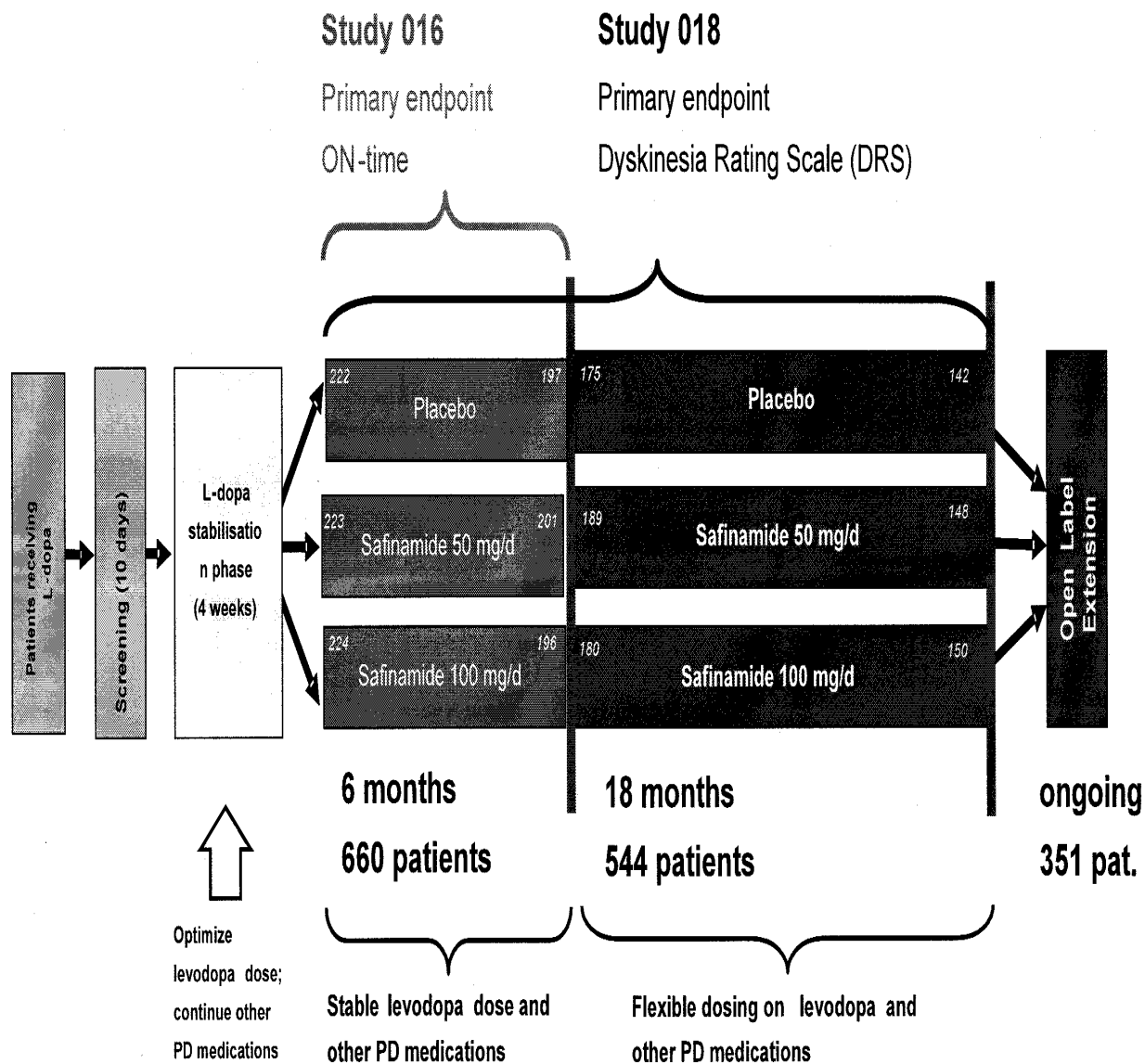
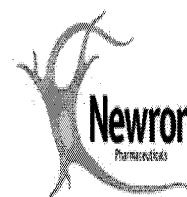
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- A double-blind, placebo controlled 18 months extension study of phase 3 pivotal study 016 (study 018 is not a pivotal study)
- To assess 2 year safety and efficacy of 50 and 100 mg safinamide/day as add-on therapy to stable L-dopa in PD patients with motor fluctuations

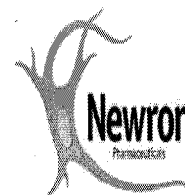
# Study design 016 and 018

*Double-blind, placebo controlled study through 2 years*



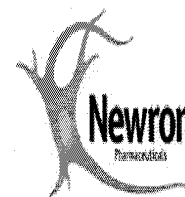
# Study 018 - Secondary endpoints

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- Change in “On-time” (ON + ON with minor dyskinesia) from baseline of study 016
- Change in individual diary categories compared to baseline of study 016
  - Improvement in ON time + ON time with minor dyskinesia with no increase in troublesome dyskinesia with respect to the 016 baseline
  - Lack of worsening ( $\leq 30$  mins) in ON time + ON time with minor dyskinesia with no increase in troublesome dyskinesia with respect to the 016 baseline
- Diary responder rate at 12-, 18-, and 24-months on the ITT and mITT, and on those who completed 24 months treatment period)
- UPDRS part IV (total and dyskinesia sub-items 32-35 and 32-24)
- Time to develop troublesome dyskinesia ( $\geq 30$  minutes increase compared to baseline)
- Time to develop any (minor + troublesome) dyskinesia ( $\geq 30$  minutes increase compared to baseline)
- Change in ADLs during ON-time (UPDRS part II) compared to placebo
- Maintenance of effects in UPDRS part II responders ( $\geq 20\%$  improvement from baseline to 016 endpoint)
- Percentage of change in L-dopa dose
- Percentage of change in any anti-PD dose
- Change in motor symptoms (UPDRS part III)
- CGI – change from baseline – mean score in the course of the study
- CGI – severity of illness – mean change from baseline to endpoint

# Study 016/018 – Parkinson's disease baseline characteristics



	Placebo (n=222)	Safinamide 50 mg/day (n=223)	Safinamide 100 mg/day (n=224)
Baseline OFF time (hours) (SD)	5.3 (2.06)	5.2 (2.08)	5.2 (2.16)
Baseline ON time (hours) (SD)	9.30 (2.155)	9.37 (2.259)	9.52 (2.426)
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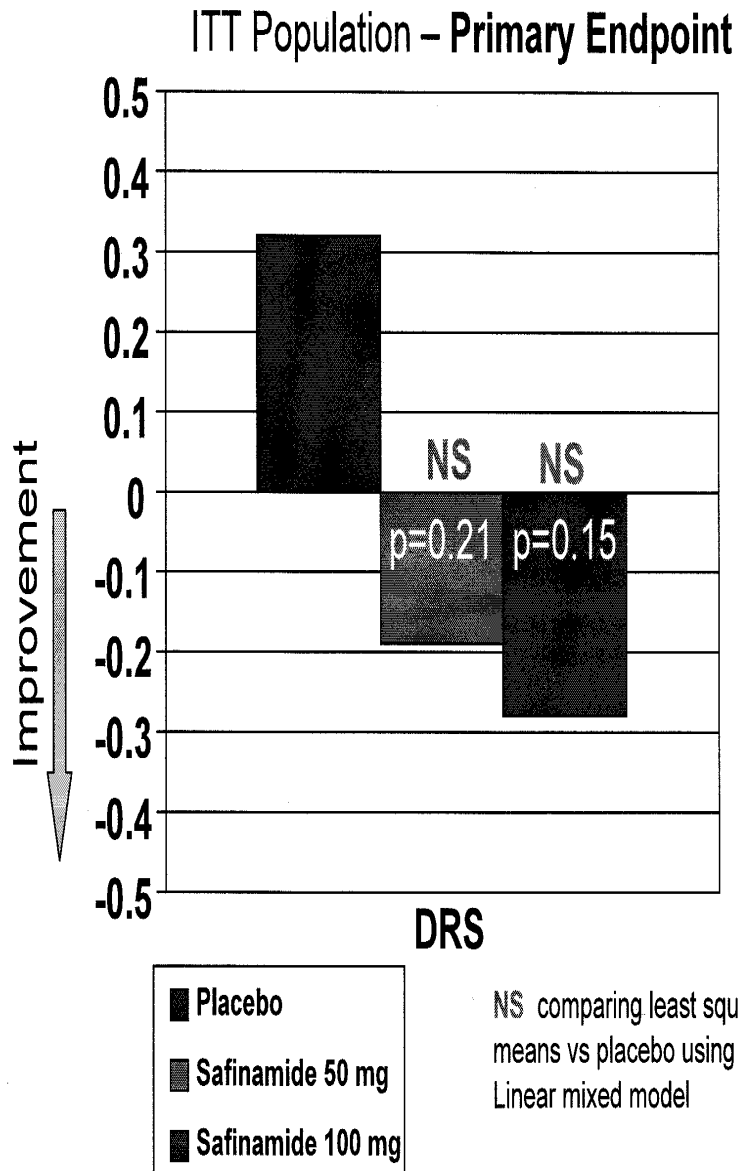
Source reference: Tables 30.1 - 33 -25.3 - 12.2

# Dyskinesia Rating Scale (DRS)

*Primary endpoint not met - Sub-sequential pre-specified endpoints considered as exploratory*



After 24 months, non-statistically significant mean improvements of 0.19 and 0.28 in the DRS score were observed in patients who received safinamide 50 mg and 100 mg respectively, versus a worsening of 0.32 for the placebo group (respectively  $p=0.21$  and  $p=0.15$  versus placebo)

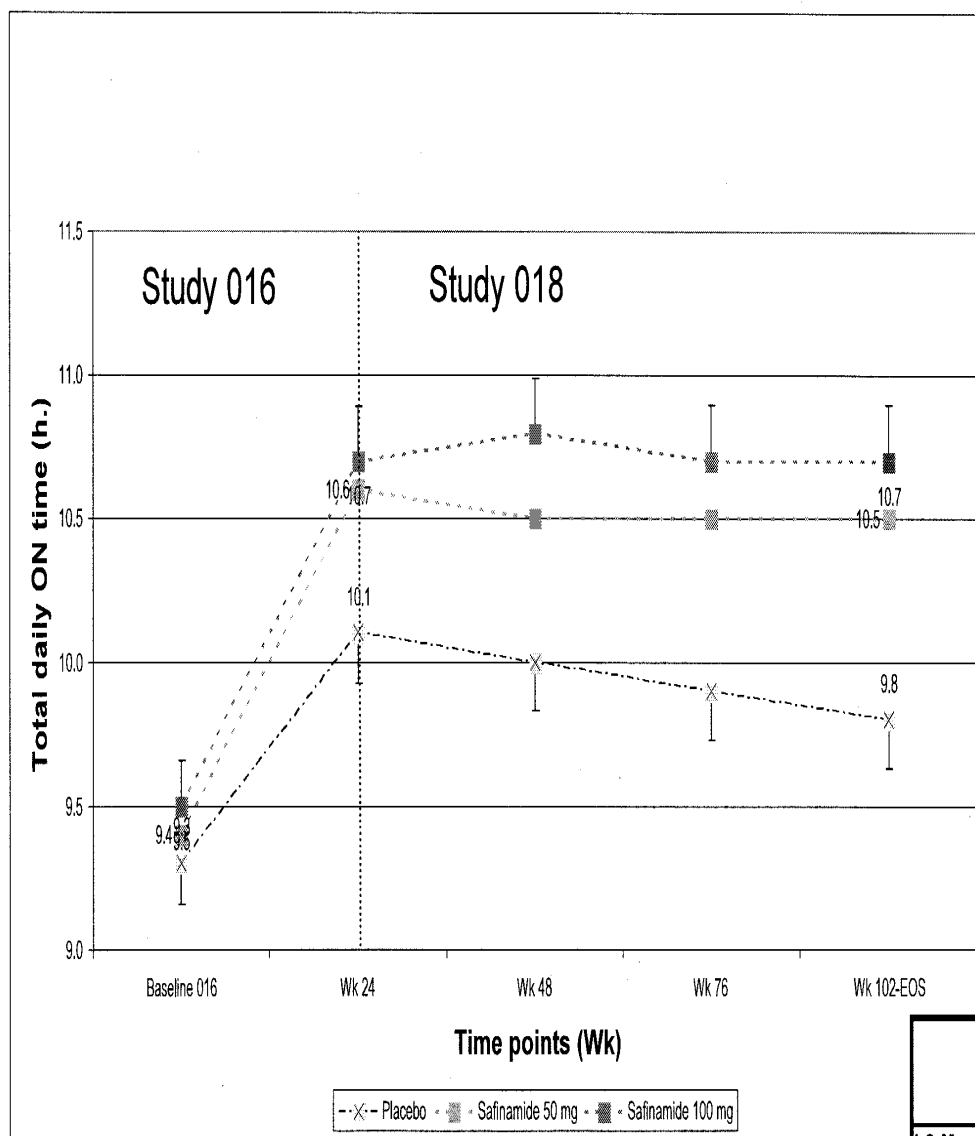
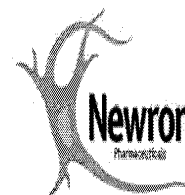




# Main secondary endpoint: ON time

(primary endpoint 016)

*Maintained clinical effect over 2 years (exploratory analysis)*



	Safinamide 50 mg/day	Safinamide 100 mg/day
LS Mean	1.01	1.18
LS Diff vs Placebo	0.67	0.83
95% CI of LS Diff	(0.23,1.11)	(0.39,1.27)
p-value vs Placebo	0.0031	0.0002

Safinamide study 018 top-line results

# Additional secondary endpoints

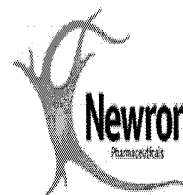
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- Significant benefit of the 100 mg/day dose on:
  - Activities of daily living (UPDRS II)
  - Motor symptoms (UPDRS III)
  - Complications of dopaminergic treatment (UPDRS IV)
  - Symptoms of depression (GRID HAMD)
  - Quality of life (PDQ-39)at the two year-endpoint
- Full study results will be submitted for presentation at upcoming scientific meetings

# Study 018 supports safety profile of safinamide on long-term

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## Adverse Events

- Serious adverse events, clinically notable events among both treatment groups in the study (50 mg and 100 mg/d) were comparable with those in the placebo group

## Drop Outs

- There were approx. 80% completers across the 3 groups

# Prospect

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- These long-term treatment results are encouraging because they support the safety profile of safinamide and results of an exploratory analysis of its effect on motor function were consistent with the effect observed in the six-month study in this advanced Parkinson's disease population
- These results may offer new hope to patients with Parkinson's disease as they need to take medications for long periods of time
- The effect of safinamide on dyskinesia will be further explored in an ongoing dedicated pilot study